REMARKS

Claims 1-17, 27, 28, 31, 32, 35, 36, 39 and 41 are pending in the application. Claims 1-17, 27, 28, 31, 32, 35, 36, 39 and 41 are rejected. No claims are allowed.

Claim 1 has been amended to more particularly define the subject matter Applicants consider their invention. Specifically, claim 1 has been amended to specify that the first arm of the dendrimer comprises a label "providing a directly detectable signal," such that binding results in the generation of a "directly detectable" hybridization pattern on the microarray. Support for the amendment can be found at least at page 13, paragraph two, of the specification as originally filed. Claim 1 has also been amended to delete "on said microarray" from step 3).

Claims 1-17, 27, 28, 31, 32, 35, 36, 39 and 41 are presented for further proceedings. Reconsideration of the claim rejections and allowance of the pending claims in view of the following remarks are respectfully requested.

Claim Rejections – 35 U.S.C. § 112

Claims 1-17, 27, 28, 31, 32, 35, 36, 39 and 41 are rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the written description requirement. According to the Examiner:

> Claim 1 includes steps "3) mixing said first and second components on said microarray" and step "5) wherein said first component comprising cDNA reagents is hybridized in a single step to both said microarray and to said second component comprising dendrimer". These steps are not supported by the specification or by the claims as originally filed. The specification teaches, at most, pre-hybridization of the first and second components (the cDNA and dendrimer), followed by hybridization to the array (see Figure 2). Regarding the issue of a single step of hybridization, the specification states "The hybridization

> speed and efficiency is greatly enhanced by **first hybridizing the cDNA to the dendrimer probes before hybridizing the cDNA to the microarray.** This single-step hybridization process also reduces the number of hybridization buffers to one by eliminating the use of a cDNA hybridization buffer" (paragraph 56, emphasis added). The passage cited above does not teach a single step of hybridization, it teaches a first step of pre-hybridization, followed by hybridization to the array. There is no other teaching in the specification which supports the mixing or hybridization of the components on the array.

Claim 1 has been amended to delete "on said microarray" from step 3), thereby rendering the rejection with respect to this limitation moot. With respect to "wherein said first component comprising cDNA reagents is hybridized in a single step to both said microarray and to said second component comprising dendrimer" in step 5), Applicants respectfully submit that the Examiner has taken an overly restrictive view of the disclosure. Although portions of the disclosure are devoted to teaching prehybridization of the cDNA reagent to the dendrimer (including cancelled claim 18 as originally filed), other portions specifically exclude mention of prehybridization. Indeed, Claim 1 itself makes no mention of "prehybridization." Furthermore, in the embodiment spanning pages 6-7, step 2) recites mixing the cDNA reagent and the dendrimer at a temperature and for a time to enable binding, while step 3) recites incubating this mixture with a microarray. The term "prehybridized" does not appear in this embodiment (contrast this with step 3) of the embodiment just below on page 7). Thus, this portion of the disclosure is consistent with mixing the cDNA reagent and the dendrimer at a temperature and for a time to enable binding is done on the microarray, such that the cDNA reagent is hybridized in a single step to both the microarray and the dendrimer. Furthermore, the specification notes that "it is to be understood that the invention is not

limited to the particular embodiments of the invention described below." Thus, one of skill in the art would recognize that the invention disclosed encompasses both prehybridization of the cDNA reagent and the dendrimer and simultaneous hybridization of the cDNA reagent to both the microarray and the dendrimer.

Accordingly, Applicants submit that claims 1-17, 27, 28, 31, 32, 35, 36, 39 and 41 comply with the written description requirement, and reconsideration of this basis for rejection is respectfully requested.

Claim Rejections – 35 U.S.C. § 103

a. Claims 1, 2, 5, 7-11, 13, 35, 36, 39 and 41 are rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Sampson et al., GB 2332516 ("Sampson") in view of Nilsen et al., US 5,487,973 ("Nilsen") and Ranki et al., US 4,563,419 ("Ranki"). With regard to claim 1, the only remaining independent claim, the Examiner believes that Figure 1 of Sampson substantially discloses the claimed invention. In particular, the Examiner states that Figure 1 of Sampson shows "wherein said first component comprising cDNA reagent is simultaneously hybridized in a single step to both said microarray and to said second component, while said first component comprising cDNA is on said microarray (Figure 1, step 2, where the cDNA reagent is combined with a second component; p. 9, lines 28 to p. 10, line 9, where tagged cDNA is hybridized to the surface of an array and the signal generated is detected; and where the hybridization between the cDNA and the array occurs as a single step)." The Examiner acknowledges that Sampson does not teach use of dendrimers, but asserts that it would have been obvious to use the dendrimers disclosed in Nilsen in the method of Sampson. The Examiner further acknowledges that neither Sampson nor Nilsen teaches that the

cDNA and dendrimer are simultaneously hybridized to the array in a single step, but asserts that it would have been obvious to do so in view of the sandwich assay disclosed in Ranki.

Applicants respectfully traverse this basis for rejection.

In rejecting claims under 35 U.S.C. § 103, it is incumbent upon the Examiner to establish a factual basis to support the legal conclusion of obviousness. *See In re Fine*, 837 F.2d 1071, 1073 (Fed. Cir. 1988). In so doing, the Examiner must make the factual determinations set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 17 (1966), *viz.*, (1) the scope and content of the prior art; (2) the differences between the prior art and the claims at issue; and (3) the level of ordinary skill in the art. "[T]he examiner bears the initial burden, on review of the prior art or on any other ground, of presenting a *prima facie* case of unpatentability." *In re Oetiker*, 977 F.2d 1443, 1445 (Fed. Cir. 1992). To establish a *prima facie* case of obviousness, all the claim limitations must be taught or suggested by the prior art. *See In re Royka*, 490 F.2d 981, 985 (CCPA 1974). Furthermore, although the analysis need not identify explicit teachings directed to the claimed subject matter, "it can be important to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does." *KSR Int'l Co. v. Teleflex Inc.*, 127 S. Ct. 1727, 1741 (2007). As such, "'there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness.'" *Id.* (quoting *In re Kahn*, 441 F.3d 977, 988 (Fed. Cir. 2006)).

Claim 1 (and thus claims 2, 5, 7-11, 13, 35, 36, 39, 41 dependent thereon) is directed to a method for detection and assay on a microarray, said method comprising,

inter alia, mixing cDNA having a capture sequence with a dendrimer having at least one first arm comprising a label and at least one second arm having a second nucleotide sequence complementary to the capture sequence, and incubating this mixture with a microarray comprising particular nucleotide sequences capable of binding to the cDNA, wherein the cDNA is hybridized in a single step to both the microarray and the dendrimer. The mixture and microarray are mixed at a temperature and for a time sufficient to allow the cDNA to bind to both the microarray and dendrimer, resulting in the generation of a directly detectable hybridization pattern on the microarray.

As explained in Applicants' previous submission, and as acknowledged by the Examiner, Sampson does not disclose hybridization of cDNA in a single step to both a microarray and to a second component. Figure 1 of Sampson shows incorporation of repeating signal amplification sequences onto cDNA using rolling circle DNA synthesis. In step 1, cDNA is synthesized from mRNA using a bi-directional primer. In step 2, the bi-directional primer is used to synthesize repeating signal amplification sequences using a circular DNA template (which the Examiner believes corresponds to the claimed "second component"). In step 3, the cDNA is hybridized to an array. Steps 2 and 3 are clearly not done simultaneously in a single step. Indeed, it is impossible to perform steps 2 and 3 together since the conditions for DNA replication are different from those for array hybridization.

In addition, claim 1 has been amended to specify that dendrimer has at least one first arm comprising a label "providing a directly detectable signal," such that binding results in the generation of a "directly detectable" hybridization pattern on the microarray. In contrast, the circular DNA template in Sampson (which the Examiner believes

corresponds to the dendrimer) is not labeled, and therefore cannot generate a directly detectable hybridization signal. DNA replication is needed to provide the signal amplification signal. *See* Figure 1. Accordingly, this feature provides a further distinction over Sampson.

Nilsen and Ranki do not cure the deficiencies of Sampson. According to the Examiner, Nilsen teaches detection of nucleic acids on arrays using dendrimer probes. However, as shown in Figures 5 and 6 of Nilsen, beads A and B are prehybridized together prior to hybridization to the array. Thus, as with Sampson, cDNA in Nilsen is not hybridized in a single step to both the microarray and the dendrimer. In fact, cDNA is not hybridized at all to an array in Nilsen. As shown in Figure 6, the nucleic acid sequence to be detected hybridizes between beads A and B – it never hybridizes to the array. Also, contrary to step 2) of instant claim 1, the nucleic acid sequences to be detected, shown in Figure 6 of Nilsen, do not contain a common capture sequence for hybridizing to the dendrimer. Rather, beads A and B each contain arms containing sequences for hybridizing with the nucleic acid sequence to be detected, upon which a bridge is formed between the two beads. *See* col. 14, lines 30-37. Thus, the nucleic acids to be detected are hybridized to the dendrimers via unique sequences – no common capture sequence is used.

Ranki is directed to a one step hybridization technique for the detection of nucleic acids from microbes. The technique involves the simultaneous hybridization of two purified single-stranded nucleic acid fragments for each microbe to be identified. One fragment is affixed onto a solid carrier, while the other fragment is labeled. These fragments are simultaneously contacted with single-stranded microbial nucleic acid,

resulting in the formation of detectable double-stranded hybrids. *See* col. 2, lines 25-49. According to the Examiner, the first fragment corresponds to the probes on the array of Sampson, and the second fragment corresponds to the dendrimer of Nilsen. The problem with the Examiner's analogy, however, is that the nucleic acids intended to be identified in Ranki, which the Examiner believes corresponds to the cDNA in Sampson (and thus also to the instantly claimed cDNA reagents), do not contain a common capture sequence. Rather, the labeled fragment hybridizes to unique sequences for each microbial nucleic acid intended to be identified. This means that different labeled fragments must be provided for each assay. This is quite different than the instantly claimed dendrimers, which can bind to any of the cDNAs having the common capture sequence. Furthermore, since each assay in Ranki is intended to identify a single microbial nucleic acid, any microarray involved in Ranki's system would not contain a plurality of features comprising particular nucleotides sequences, but rather only one.

Thus, overall, there would have been no logical basis for combining the cited references in the manner suggested by the Examiner, nor a reasonable likelihood of success at arriving at the instantly claimed invention. Accordingly, Applicants submit that claims 1, 2, 5, 7-11, 13, 35, 36, 39, 41 are not unpatentable over Sampson in view of Nilsen and Ranki, and reconsideration of this basis for rejection is respectfully requested.

b. Claims 3, 4, 16, 17, 19 and 23-26 are rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over Sampson in view of Nilsen and Rinki as applied above, and further in view of Combates et al., US 6,045,998 ("Combates"). Claims 19 and 23-26 were previously cancelled, thereby rendering the rejection with respect to this claim moot. With regard to the remaining claims, each of claims 3, 4, 16 and 17 depends from

claim 1. As discussed above with respect to the rejection of claim 1, the combination of Sampson with Nilsen and Ranki would not have suggested hybridization of cDNA in a single step to both a microarray and dendrimer. The Examiner has pointed to nothing in Combates that remedies the deficiencies of Sampson, Nilsen and Ranki in this respect. As such, the combination of Combates with Sampson, Nilsen and Ranki cannot render the claimed invention obvious. *See In re Rijckaert*, 9 F.3d 1531, 1533 (Fed Cir. 1993).

Accordingly, Applicants submit that claims 3, 4, 16 and 17 are not unpatentable over Sampson in view of Nilsen and Ranki, and further in view of Combates, and reconsideration of this basis for rejection is respectfully requested.

c. Claim 6 is rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over Sampson in view of Nilsen and Ranki as applied above, and further in view of Kool et al., US 5,714,320 ("Kool"). Claim 6 depends from claim 1. As discussed above with respect to the rejection of claim 1, the combination of Sampson with Nilsen and Ranki would not have suggested hybridization of cDNA in a single step to both a microarray and dendrimer. The Examiner has pointed to nothing in Kool that remedies the deficiencies of Sampson, Nilsen and Ranki in this respect. As such, the combination of Kool with Sampson, Nilsen and Ranki cannot render the claimed invention obvious. *See Rijckaert*, 9 F.3d at 1533.

Accordingly, Applicants submit that claim 6 is not unpatentable over Sampson in view of Nilsen and Ranki, and further in view of Kool, and reconsideration of this basis for rejection is respectfully requested.

d. Claims 12-15 are rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over Sampson in view of Nilsen and Ranki as applied above, and further in

view of Wang et al., US 6,004,775 ("Wang"). Each of claims 12-15 depend from claim 1. As discussed above with respect to the rejection of claim 1, the combination of Sampson with Nilsen and Ranki would not have suggested hybridization of cDNA in a single step to both a microarray and dendrimer. The Examiner has pointed to nothing in Wang that remedies the deficiencies of Sampson, Nilsen and Ranki in this respect. As such, the combination of Wang with Sampson, Nilsen and Ranki cannot render the claimed invention obvious. *See Rijckaert*, 9 F.3d at 1533.

Accordingly, Applicants submit that claims 12-15 are not unpatentable over Sampson in view of Nilsen and Ranki, and further in view of Wang, and reconsideration of this basis for rejection is respectfully requested.

e. Claims 27, 28, 31 and 32 are rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over Sampson in view of Nilsen and Ranki as applied above, and further in view of Brenner et al., US 5,846,719 ("Brenner"). Each of claims 27, 28, 31 and 32 depends from claim 1. As discussed above with respect to the rejection of claim 1, the combination of Sampson with Nilsen and Ranki would not have suggested hybridization of cDNA in a single step to both a microarray and dendrimerThe Examiner has pointed to nothing in Brenner that remedies the deficiencies of Sampson, Nilsen and Ranki in this respect. As such, the combination of Brenner with Sampson, Nilsen and Ranki cannot render the claimed invention obvious. *See Rijckaert*, 9 F.3d at 1533.

Accordingly, Applicants submit that claims 27, 28, 31 and 32 are not unpatentable over Sampson in view of Nilsen and Ranki, and further in view of Brenner, and reconsideration of this basis for rejection is respectfully requested.

CONCLUSION

It is believed that claims 1-17, 27, 28, 31, 32, 35, 36, 39 and 41 are now in condition for allowance, early notice of which would be appreciated. If any additional fees are due, the Commissioner is authorized to charge any such fee to our Deposit Account No. 50-3329. Please contact the undersigned if any further issues remain to be addressed in connection with this submission.

Dated: August 11, 2010

Respectfully submitted,

/Kenneth M. Zeidner, Reg. No. 64700/
Kenneth M. Zeidner
Reg. No. 64,700

Diehl Servilla LLC
77 Brant Avenue, Suite 210
Clark, New Jersey 07066
TEL (732) 815-0404
FAX (732) 815-1330
Attorneys for Applicants